Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) A nucleic acid-lipid particle composition for introducing a nucleic acid into a cell, said particle composition comprising:

(a) a nucleic acid-lipid particle comprising a cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a nucleic acid, wherein said nucleic acid is encapsulated in a lipid bilayer of said nucleic acid-lipid particle, and wherein said conjugated lipid that inhibits aggregation of particles is a member selected from the group consisting of a PEG-lipid, an ATTA-lipid and a cationic-polymer-lipid conjugate having the formula

A——W——Y

I

wherein:

A is a lipid moiety;

W is a hydrophilic polymer; and

Y is a polycationic moiety; and

(b) an endosomal membrane destabilizer, wherein said endosomal membrane destabilizer is Ca^{++} ion.

2. (Original) The nucleic acid–lipid particle composition of claim 1, wherein said endosomal membrane destabilizer is outside said nucleic acid-lipid particle.

3. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said endosomal membrane destabilizer is both outside and inside said nucleic acid-lipid particle.

4. (Canceled)

5. (Original) The nucleic acid-lipid particle composition of claim 4, wherein the concentration of Ca^{++} ion is from about 0.1 mM to about 100 mM.

6. (Original) The nucleic acid-lipid particle composition of claim 5, wherein the concentration of Ca^{++} ion is from about 1 mM to about 20 mM.

7. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said particle has a median diameter of less than about 150 nm.

8. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said cationic lipid is a member selected from the group consisting of N,N-dioleyl-N,N-dimethylammonium chloride (DODAC), N,N-distearyl-N,N-dimethylammonium bromide (DDAB), N-(1-(2,3-dioleoyloxyl)propyl)-N,N,N-trimethylammonium chloride (DOTAP), N-(1-(2,3-dioleyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTMA), and N,N-dimethyl-2,3-dioleyloxy)propylamine (DODMA), and combinations thereof.

9. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said particle further comprises an additional noncationic lipid.

10. (Original) The nucleic acid-lipid particle composition of claim 9, wherein said noncationic lipid is selected from the group consisting of DOPE, POPC, and EPC.

11. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said particle comprises a functional group that facilitates Ca^{++} ion chelation.

12. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said conjugated lipid that inhibits aggregation of particles has the formula

A——W——Y

I

wherein:

A is a lipid moiety;

W is a hydrophilic polymer; and

Y is a polycationic moiety.

13. (Original) The nucleic acid-lipid particle composition of claim 12, wherein W is a polymer selected from the group consisting of PEG, polymide, polylactic acid, polyglycolic acid, polylactic acid/polyglycolic acid copolymers and combinations thereof, said polymer having a molecular weight of about 250 to about 7000 daltons.

14. (Original) The nucleic acid-lipid particle composition of claim 12, wherein Y has at least 4 positive charges at a selected pH.

15. (Original) The nucleic acid-lipid particle composition of claim 12, wherein Y is a member selected from the group consisting of lysine, arginine, asparagine, glutamine, derivatives thereof and combinations thereof.

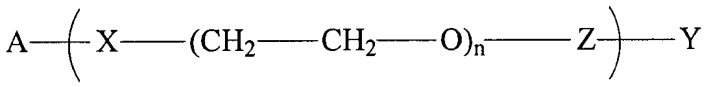
16. (Original) The nucleic acid-lipid particle composition of claim 12, wherein A is a member selected from the group consisting of a diacylglycerolyl moiety, a dialkylglycerolyl moiety, a N-N-dialkylamino moiety, a 1,2-diacyloxy-3-aminopropane moiety and a 1,2-dialkyl-3-aminopropane moiety.

17. (Original) The nucleic acid-lipid particle composition of claim 12, wherein W is PEG.

18. (Original) The nucleic acid-lipid particle composition of claim 12, wherein W is a polyamide polymer.

19. (Original) The nucleic acid-lipid particle composition of claim 12, wherein W has a molecular weight of about 250 to about 2000 daltons.

20. (Original) The nucleic acid-lipid particle composition of claim 17, having the general structure of Formula II:



II

wherein

X is a member selected from the group consisting of a single bond or a functional group covalently attaching said lipid to at least one ethylene oxide unit;

Z is a member selected from the group consisting of a single bond or a functional group covalently attaching said at least one ethylene oxide unit to a cationic group; and

n is an integer having a value of between about 6 to about 50.

21. (Original) The nucleic acid-lipid particle composition of claim 20, wherein X is a member selected from the group consisting of a single bond, phosphatidylethanolamino, phosphatidylethanolamido, phosphoro, phospho, phosphatidylethanolamino, phosphoethanolamido, carbonyl, carbamate, carboxyl, carbonate, amido, thioamido, oxygen, sulfur and NR, wherein R is a hydrogen or alkyl group.

22. (Original) The nucleic acid-lipid particle composition of claim 20, wherein

Z is a member selected from the group consisting of a single bond, phosphatidylethanolamino, phosphatidylethanolamido, phosphoro, phospho, phosphoethanolamino, phosphoethanolamido, carbonyl, carbamate, carboxyl, carbonate, amido, thioamido, oxygen, sulfur and NR, wherein R is a hydrogen or alkyl group.

23. (Original) The nucleic acid-lipid particle composition of claim 20, wherein

A is a diacylglycerolyl moiety;

X is a phosphoethanolamido;

Z is NR, wherein R is a hydrogen atom; and

Y is a member selected from the group consisting of about 1 to about 10 basic amino acids or derivatives thereof.

24. (Original) The nucleic acid-lipid particle composition of claim 23, wherein

A is a diacylgercerolyl moiety having 2 fatty acyl chains, wherein each acyl chain is independently between 2 and 30 carbons in length and is either saturated or has varying degrees of saturation.

25. (Currently Amended) The nucleic acid-lipid particle composition of claim ~~23~~1 or claim 20, wherein Y is a member selected from the group consisting of lysine, arginine, asparagine, glutamine, derivatives thereof and combinations thereof.

26. (Original) The nucleic acid-lipid particle composition of claim 23, wherein

A is a diacylgercerolyl moiety having 2 fatty acyl chains, wherein each acyl chain is a saturated C-18 carbon chain; and

Y is a cationic group having 4 lysine residues or derivatives thereof.

27. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said conjugated lipid that inhibits aggregation of particles is a PEG-lipid.

28. (Original) The nucleic acid-lipid particle composition of claim 27, wherein said PEG-lipid is PEG-ceramide.

29. (Original) The nucleic acid-lipid particle composition of claim 28, wherein the ceramide of said PEG-ceramide comprises a fatty acid group having about 8 to about 20 carbon atoms.

30. (Original) The nucleic acid-lipid particle composition of claim 28, wherein said PEG-lipid is PEG-phosphatidylethanolamine.

31. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said conjugated lipid that inhibits aggregation of particles is an ATTA-lipid.

32. (Original) The nucleic acid-lipid particle composition of claim 1, wherein said nucleic acid is selected from the group consisting of a plasmid, an antisense oligonucleotide, and a ribozyme.

33. (Previously Presented) A method of introducing a nucleic acid into a cell, said method comprising:

contacting said cell with a nucleic acid-lipid particle composition, said particle composition comprising:

(a) a nucleic acid-lipid particle comprising a cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a nucleic acid, wherein said nucleic acid is encapsulated in a lipid bilayer of said nucleic acid-lipid particle, and wherein said

conjugated lipid that inhibits aggregation of particles is a member selected from the group consisting of a PEG-lipid, an ATTA-lipid and a cationic-polymer-lipid conjugate having the formula

A——W——Y

I

wherein

A is a lipid moiety;

W is a hydrophilic polymer; and

Y is a polycationic moiety; and

(b) an endosomal membrane destabilizer, wherein said endosomal membrane destabilizer is Ca^{++} ion.

34. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said endosomal membrane destabilizer is outside said nucleic acid-lipid particle.

35. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said endosomal membrane destabilizer is Ca^{++} ion.

36. (Original) The method of introducing a nucleic acid into a cell of claim 35, wherein the concentration of Ca^{++} ion is from about 0.1 mM to about 100 mM.

37. (Original) The method of introducing a nucleic acid into a cell of claim 36, wherein the concentration of Ca^{++} ion is from about 1 mM to about 20 mM.

38. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said particle has a median diameter of less than about 150 nm.

39. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said cationic lipid is a member selected from a group consisting of N,N-dioleyl-N,N-dimethylammonium chloride (DODAC), N,N-distearyl-N,N-dimethylammonium bromide (DDAB), N-(1-(2,3-dioleoyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTAP), N-(1-(2,3-dioleyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTMA), and N,N-dimethyl-2,3-dioleyloxy)propylamine (DODMA) and combinations thereof.

40. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said particle further comprises an additional noncationic lipid.

41. (Original) The method of introducing a nucleic acid into a cell of claim 40, wherein said noncationic lipid is selected from the group consisting of DOPE, POPC, and EPC.

42. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said particle comprises a functional group that facilitates Ca^{++} ion chelation.

43. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said conjugated lipid that inhibits aggregation of particles has the formula

A——W——Y

I

wherein

A is a lipid moiety;

W is a hydrophilic polymer; and

Y is a polycationic moiety; and

44. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein W is a polymer selected from the group consisting of PEG, polyamide, polylactic acid, polyglycolic acid, polylactic acid/polyglycolic acid copolymers and

combinations thereof, said polymer having a molecular weight of about 250 to about 7000 daltons.

45. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein Y has at least 4 positive charges at a selected pH.

46. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein Y is a member selected from the group consisting of lysine, arginine, asparagine, glutamine, derivatives thereof and combinations thereof.

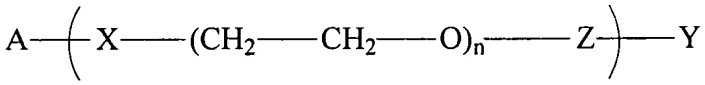
47. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein A is a member selected from the group consisting of a diacylglycerolyl moiety, a dialkylglycerolyl moiety, a N-N-dialkylamino moiety, a 1,2-diacyloxy-3-aminopropane moiety and a 1,2-diakyl-3-aminopropane moiety.

48. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein W is PEG.

49. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein W is a polyamide polymer.

50. (Original) The method of introducing a nucleic acid into a cell of claim 43, wherein W has a molecular weight of about 250 to 2000 daltons.

51. (Original) The method of introducing a nucleic acid into a cell of claim 48, having the general structure of Formula II:



II

wherein

X is a member selected from the group consisting of a single bond or a functional group covalently attaching said lipid to at least one ethylene oxide unit;

Z is a member selected from the group consisting of a single bond or a functional group covalently attaching said at least one ethylene oxide unit to a cationic group; and

n is an integer having a value of between about 5 to about 50.

52. (Original) The method of introducing a nucleic acid into a cell of claim 51, wherein

X is a member selected from the group consisting of a single bond, phosphatidylethanolamino, phosphatidylethanolamido, phosphoro, phospho, phosphoethanolamino, phosphoethanolamido, carbonyl, carbamate, carboxyl, carbonate, amido, thioamido, oxygen, sulfur and NR, wherein R is a hydrogen or alkyl group.

53. (Original) The method of introducing a nucleic acid into a cell of claim 51, wherein

Z is a member selected from a group consisting of a single bond, phosphatidylethanolamino, phosphatidylethanolamido, phosphoro, phospho, phosphoethanolamino, phosphoethanolamido, carbonyl, carbamate, carboxyl, carbonate, amido, thioamido, oxygen, sulfur and NR, wherein R is a hydrogen or alkyl group.

54. (Original) The method of introducing a nucleic acid into a cell of claim 51, wherein

A is a diacylglycerolyl moiety;

X is phosphoethanolamido;

Z is NR, wherein R is a hydrogen atom; and

Y is a member selected from the group consisting of about 1 to about 10 basic amino acids or derivatives thereof.

55. (Original) The method of introducing a nucleic acid into a cell of claim 54, wherein

A is a diacylgercerolyl moiety having 2 fatty acyl chains, wherein each acyl chain is independently between 2 and 30 carbons in length and is either saturated or has varying degrees of saturation.

56. (Currently Amended) The method of introducing a nucleic acid into a cell of claim ~~54~~33 or claim 51, wherein

Y is a member selected from the group consisting of lysine, arginine, asparagine, glutamine, derivatives thereof and combinations thereof.

57. (Original) The method of introducing a nucleic acid into a cell of claim 54, wherein

A is a diacylgercerolyl moiety having 2 fatty acyl chains, wherein each acyl chain is a saturated C-18 carbon chain; and

Y is a cationic group having 4 lysine residues or derivatives thereof.

58. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said conjugated lipid that inhibits aggregation of particles is a PEG-lipid.

59. (Original) The method of introducing a nucleic acid into a cell of claim 58, wherein said PEG-lipid is PEG ceramide.

60. (Original) The method of introducing a nucleic acid into a cell of claim 59, wherein the ceramide of said PEG-ceramide comprises a fatty acid group having about 8t o about 20 carbon atoms.

61. (Original) The method of introducing a nucleic acid into a cell of claim 59, wherein said PEG-lipid is PEG-phosphatidylethanolamine.

62. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said conjugated lipid that inhibits aggregation of particles is an ATTA-lipid.

63. (Original) The method of introducing a nucleic acid into a cell of claim 33, wherein said nucleic acid is selected from the group consisting of a plasmid, an antisense oligonucleotide, and a ribozyme.

64-67. (Canceled)